Re-evaluation Decision RVD2011-08

1-bromo-3-chloro-5,5-dimethylhydantoin

1,3-dichloro-5,5-dimethylhydantoin

1,3-dichloro-5-ethyl-5-methylhydantoin

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Re-evaluation Decision

After a re-evaluation of the antimicrobials, 1-bromo-3-chloro-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin, and 1,3-dichloro-5-ethyl-5-methylhydantoin (henceforth called halohydantoins), Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting continued registration of products containing these active ingredients for sale and use in Canada.

An evaluation of available scientific information found that products containing the halohydantoins do not present unacceptable risks to human health or the environment when used according to the revised label directions. As a condition of the continued registration of uses, new risk-reduction measures must be included on the labels of all products containing these active ingredients. No additional data are required at this time.

The regulatory approach for the re-evaluation of the halohydantoins was first presented in Proposed Re-evaluation Decision PRVD2011-01, *1-bromo-3chloro-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin and 1,3-dichloro-5-ethyl-5-methylhydantoin,* a consultation document.[1] This Re-evaluation Decision[2] describes this stage of the PMRA's regulatory process for the re-evaluation of the halohydantoins as well as summarizes the Agency's decision and the reasons for it. Comments received during the consultation process did not result in substantial changes to the proposed regulatory decision as described in the PRVD. Appendix I summarizes the comments and provides the PMRA's response. This decision is consistent with the proposed re-evaluation decision stated in PRVD2011-01. To comply with this decision, registrants of products containing the halohydantoins will be informed of the specific requirements affecting their product registration(s).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act.*

The three halohydantoins have been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Based on the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA has made a regulatory decision and requires appropriate risk-reduction measures for Canadian uses of the halohydantoins. In this decision, the PMRA took into account the Canadian use pattern and issues (for example, the federal Toxic Substances Management Policy [TSMP]).

The USEPA re-evaluated the halohydantoins and published its conclusions in a 2007 RED.

For more details on the information presented in this Re-evaluation Decision, please refer to the Science Evaluation in the related Proposed Re-evaluation Decision PRVD2011-01, *1-bromo-3chloro-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin and 1,3-dichloro-5-ethyl-5-methylhydantoin*.

What Are the Halohydantoins?

The three halohydantoins under re-evaluation are antimicrobials that are used to control bacterial, fungal and algal slimes in industrial recirculating water systems, pulp and paper process waters, ornamental fountains, swimming pools, spas and as an in-tank toilet sanitizer. End-use products are typically placed, poured or pumped by workers or home owners.

Health Considerations

Can Approved Uses of the Halohydantoins Affect Human Health?

The three halohydantoins under re-evaluation are unlikely to affect your health when used according to the revised label directions.

People could be exposed to the halohydantoins by consuming food and water, by handling the pesticide product or through postapplication. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that the halohydantoins were unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Environmental Considerations

What Happens When the Halohydantoins Are Introduced Into the Environment?

The three halohydantoins are unlikely to affect non-target organisms when used according to the revised label directions.

The USEPA concluded that the indoor and contained uses of the halohydantoins would not result in appreciable environmental exposure when products are used as labelled. Therefore, the USEPA did not anticipate ecological risk from these uses. Due to a similar use pattern in Canada, environmental exposure is expected to be limited and ecological risk is considered not to be of concern. The PMRA is requiring advisory label statements to prevent the release of these chemicals into the environment for the protection of non-target species.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of the halohydantoins, the PMRA is requiring further risk-reduction measures for product labels.

Human Health

- Additional statements warning about the severe skin and eye irritation properties and dermal sensitization potential of the product
- Additional protective equipment to protect handlers
- Advisory label statements to limit the use to non-food contact paper/paperboard or cans for the products that were not issued with a "no objection status" by Health Canada.

Environment

- Additional advisory label statements.

Appendix II lists all required label amendments.

Other Information

Any person may file a notice of objection[3] regarding this decision on the halohydantoins within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[3] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

1. Function, registered uses and application methods of halohydantoins.

1.1 Comment

The function, registered uses and application methods of the halohydantoins need to be clarified.

PMRA Response
Halohydantoins are antimicrobials that are used to control bacterial, fungal and algal slimes in industrial recirculating water systems (evaporative exchange water towers, heat exchange water systems, influent systems, industrial water scrubbing systems, brewery pasteurizers, and industrial air washers), pulp and paper process waters, ornamental fountains, swimming pools, spas and as an in-tank toilet sanitizer. End-use products are typically placed, poured or pumped by workers or home owners directly into the water to treat or into intermittent, slug, or continuous feeding systems.

1.2 Comment

The description of the maximum Canadian application rates of halohydantoins for swimming pools and spas needs to be clarified.

PMRA Response
Domestic products are applied at rates to achieve a maximum of 3 ppm residual bromine in residential pools using ~ 0.02 kg a.i. per 10 000 litres water, 5 ppm residual bromine in larger or heavily soiled pools using $\leq$ 0.17 kg a.i. per 10 000 litres water, and 5 ppm residual bromine in spas and hot-tubs using ~0.04 kg a.i. per 10 000 litres water.

1.3 Comment

Why are Canadian use levels higher than American use levels indicated in the USEPA RED?

PMRA Response
All Canadian use rates referred to in PRVD 2011-01 come from current Canadian halohydantoin labels. These labels are available on the PMRA label search data base: http://pr-rp.hc-sc.gc.ca/ls-re/index-eng.php. The American rates to which Canadian rates were compared come from the USEPA RED and are based on American labels.

2. Human Health Risk Assessment

2.1 Comment

Clarification is required on what the term "halohydantoins" refers to with reference to post-application exposures. Post-application exposure is primarily to 5,5-dimethylhydantoin (DMH) residual, not to the parent halohydantoin.

PMRA Response

Throughout PRVD 2011-01, "halohydantoins" refers to the parent halohydantoin molecule or its major degradates, 5,5-dimethylhydantoin (DMH) and 5-ethyl-5-methylhydantoin (EMH). The toxicity endpoints used by the USEPA for their post-application halohydantoin risk assessments and presented in Appendix III of PRVD 2011-01 are based on DMH and EMH, not the parent halohydantoin molecule.

2.2 Comment

More information is required to substantiate the claim in PRVD 2011-01 that for the Pulp and Paper Process Water occupational use scenario of placing a solid product into the system, the Canadian use rate results in a dermal MOE of <100, since this is substantially lower than the dermal MOE of 2730 presented in the RED for the same use scenario. Furthermore, the requirement for coveralls, which this result triggers, is questioned.

PMRA Response

The application rate used by the USEPA in the occupational risk assessment for the Pulp and Paper Process Water scenarios was 1.96 pounds active ingredient (a.i.) per 100 tons of paper, equivalent to 0.0098 kg a.i. per metric tonne of paper. Using the maximum Canadian label rate for Pulp and Paper Process Water uses of 0.58 kg a.i. per metric tonne of paper, the PMRA calculated MOEs for the two relevant use scenarios using the USEPA's approach: solid place (for tablet formulations) and solid pour (for granular and powder formulations). The unit exposures, quantity handled per day and NOAELs used by the PMRA were those presented in Table 6 of the USEPA's *Dihalodialkylhydantoin Occupational Residential Exposure Assessment*, available at http://www.regulations.gov (Document ID: EPA-HQ-OPP-2004-0303-0009). For comparison, the application rate and dermal MOEs from the USEPA's risk assessment and the PMRA's risk assessment are presented in the following table, for each use scenario:

			Application Rate Used in Assessment (kg a.i. / metric tonne paper)	**Dermal MOE**
Pulp and Paper Process Water	Solid Place	USEPA	0.0098	2730
		PMRA	0.58	20
	Solid Pour	USEPA	0.0098	69700
		PMRA	0.58	502

Since the resulting dermal MOE for the "solid place" scenario is 20, much lower than the level of concern of 100, coveralls are required to mitigate the risk to workers placing solids into water systems. This scenario is relevant to tablet formulations. The "solid pour" scenario encompasses all other Canadian formulations. As such, the PMRA requires that workers handling commercial products formulated as tablets for use in Pulp and Paper Process Water systems must wear coveralls in addition to the PPE required for all other products. Revised label amendments are listed in Appendix II.

2.3 Comment

Further details or reference to relevant sections of the RED are requested regarding calculations for occupational and residential exposures, risks, and MOEs for product uses.

PMRA Response
In PRVD 2011-01, all occupational risk assessments described are described in the RED, section III A 8, or in the associated *Dihalodialkylhydantoin Occupational Residential Exposure Assessment*, available at http://www.regulations.gov (Document ID: EPA-HQ-OPP-2004-0303-0009). All residential risk assessments described in the PRVD are described in the RED in section III A 6, with relevant handler scenarios described on pages 22-24 and Table 9, and relevant post-application scenarios described on pages 27-28 and Table 11.

3. Environmental Risk Assessment

PRVD 2011-01 states that the major degradates of the halohydantoins, 5,5-dimethylhydantoin (DMH) and 5-ethyl-5-methylhydantoin (EMH), are considered persistent. Clarification is required on how this conclusion was reached and on how this conclusion affected the outcome of the environmental risk assessment.

PMRA Response
The environmental fate of DMH is described in the USEPA RED. These data are also applicable to EMH, given the USEPA's conclusion that data developed on DMH are applicable to EMH and vice versa. The USEPA stated that DMH was hydrolytically stable at pH 5, pH 7 and pH 9 and therefore may leach in the soil profile or move with surface water runoff, posing potential environmental concerns. Furthermore, DMH has aqueous photolytic stability, based on a study conducted at pH 7 and 25 ± 1 °C in the presence of a xenon arc light source, which resulted in a first order rate constant of 7.89×10^{-4}/day which translates into a half life of 878 days. The USEPA stated that aqueous photolytic stability means that surface water run-off of DMH can be a source of concern for drinking water contamination. There were no available data on mobility (soil column leaching) and binding constants to soils necessary for determining whether hydantoins, including DMH and EMH, would be persistent in soils. The USEPA could not determine if hydantoins are bioaccumulative and a source of concern for aquatic organisms.

Given the Canadian use-pattern of indoor and contained uses only, and treatment of contaminated water prior to release in the environment, environmental exposure to DMH and EMH will likely be limited, and ecological risk is considered not to be of concern. Based on PMRA general practices for antimicrobial active ingredients, a standard advisory statement to prevent effluent discharge is required.

4. Proposed Environmental Label Statements

4.1 Comment

Clarification is required in the wording of the following standard environmental label statement:

> ***DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.***

"Sewer systems" is not specific: does this refer to storm sewers or sanitary sewers?

PMRA Response
This is a standard statement that can be required for commercial class products which could be discharged into water bodies and adversely affect aquatic organisms. In this statement, "sewer systems" refers to any sewers with the potential to discharge into natural bodies of water such as rivers, etc. This typically refers to storm sewers, however sanitary sewers would be included as well if they discharge into natural bodies of water.

4.2 Comment

Clarification is required in the wording of the following standard environmental label statement:

> ***DO NOT apply to any body of water***

This wording needs to be clarified since bodies of water such as swimming pools are registered use-sites.

PMRA Response
This is a standard statement that is required for all domestic class products with the exception of "ready-to-use" products. All of the halohydantoin domestic products (swimming pool and spa uses) are "ready-to-use" products, therefore, this statement is not required on the halohydantoin domestic end-use product labels and has been removed from the label amendments. Please refer to the revised label amendments in Appendix II.

Appendix II Revised Label Amendments for Products Containing 1-bromo-3 chloro-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin and 1,3-dichloro-5-ethyl-5-methylhydantoin

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements below.

The labels of the Canadian products containing 1-bromo-3 chloro-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin and 1,3-dichloro-5-ethyl-5-methylhydantoin must be revised to include the following statements to further protect workers, bystanders and the environment.

I) Add to the primary display panel of all products:

> DANGER – CORROSIVE TO EYES AND SKIN
> POTENTIAL SKIN SENSITIZER

II) Add to the **TOXICOLOGICAL INFORMATION** of all products:

> This product is corrosive to skin and eyes and may produce a sensitization response or allergic reaction in some individuals.

III) Add to the **FIRST AID** of all products:

> If irritation or other adverse effects develop, wash with soap and water immediately. Seek medical attention if symptoms persist.

IV) Add to **PRECAUTIONS**:

For all commercial end-use products:

> Wear long pants, a long-sleeved shirt, chemical-resistant gloves and goggles or a face-shield while cleaning equipment and handling product.

In addition, for all commercial end-use products formulated as tablets and registered for pulp and paper uses, add the statement:

> For pulp and paper uses, wear coveralls in addition to all other required personal protective equipment while placing the product.

For all domestic end-use products:

> It is recommended to wear rubber gloves and goggles when handling the product.

V) Add to the **DIRECTIONS FOR USE**, unless a 'no objection status' was issued by the Health Canada's Bureau of Chemical Safety:

For all commercial end-use products registered for pulp and paper uses:

> **DO NOT** use this product in the production of paper or paperboard that will come into contact with food.

For the commercial end-use product registered for use in the canning industry (Registration No. 21591):

> **DO NOT** use this product in the production of cans that will come into contact with food.

VI) Add to the **DIRECTIONS FOR USE**:

For all end-use products:

> **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

For all commercial end-use products:

> **DO NOT** discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.